In the outstanding Office Action, the Patent Office states that "Applicant is required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action."

In response to the foregoing, Applicants are submitting herewith formal drawings that are fully responsive to the Notice of Draftsperson's Patent Drawing Review. Accordingly, Applicants have complied with the Patent Office's requirement for drawing corrections.

Also in the outstanding Office Action, the Patent Office states that "[t]he listing of references in the specification is not a proper information disclosure statement." The Patent Office then goes on to say that "unless the references have been cited by the examiner on form PTO-892, they have not been considered."

In view of the foregoing, Applicants are submitting herewith a formal Information Disclosure Statement in which several of the references disclosed in the specification are included.

Claims 1-50 stand rejected under 35 U.S.C. 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In support of the rejection, the Patent Office states that "[i]t would constitute undue experimentation to practice the invention as claimed...." In particular, the Patent Office states the following:

> The instant application lacks any amount or direction as to the practice of generating useful "expert rules" for disease analysis as seen in claim 1, lines 8-9 (also claims 2, 14, 16, 28, 29, and 40). The specification does not provide or suggest any rules for a disease or medical condition evaluation, particularly with respect to disease association with methylation status. The examples provided are only a generic description of the claimed method. None of the examples

provide a description of what was used as the "expert rules" for evaluation and selection of a disease type or medical condition. The prior art does not teach any common rules. In addition, the applicant has defined a global problem to be solved, disease analysis for guiding the selection of therapeutic treatment regimens, but no guidance on how to implement these rules, particularly for the claimed purposes. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of detailed working examples in the specification, and the unpredictability of evaluating a disease type or medical condition, the specification, as filed is not enabling for the method of using "expert rules" for disease analysis as claimed. As such, claims drawn to the use of "expert rules" are not enabled.

The instant application lacks any amount or direction as to the practice the process of "selecting a type of disease or medical condition based on the methylation status..." as in lines 9-10 of claim 1 (also claims 14, 28 and 40). The specification does not provide or suggest any parameters within which the selection is to be practiced, nor from what list the selection is being selected from. The description does not provide or suggest the contents of the data being selected from, nor a library database in which the gathered data consists of appropriate information sufficient for statistical purposes that would result in a meaningful and useful result. One of skill in the art would not reasonably be able to determine the parameters of the selection process based on a patient's methylation status; whether the selection must be a perfect match or if not an exact match then the thresholds for the selection are not clear or direct. The prior art does not teach any common process of disease selection. The generic examples are not actual reductions to practice for any aspect of the invention. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of detailed working examples in the specification, and the unpredictability of selecting a type of disease or medical condition, the specification, as filed is not enabling for the process or selection as claimed. As such, claims drawn to the use of the selected disease type or medical condition are not enabled.

The instant application lacks any amount or direction as to the process of generating a "ranked listing of diseases [...] based on the information about the methylation status [...]" lines 11-12 of claim 1

> (also claims 14, 28 and 40). Nowhere in the claims or the specification is there a clear and direct explanation as to how the stated elements are to be ranked. The specification does not provide or suggest any parameters with which the diseases are to be ranked. The description does not provide or suggest the contents of the data on the disease being ranked, nor a library database in which the gathered data consists of appropriate information sufficient for statistical purposes that would result in a meaningful and useful result. One of skill in the art would not reasonably be able to determine the parameters of the ranked listing process based on a patient's methylation status. The prior art does not teach any common process of disease rank, particularly in association with methylation status. The generic examples are not actual reductions to practice for any aspect of the invention. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of detailed working examples in the specification, and the unpredictability of ranking a list of diseases, the specification, as filed is not enabling for the process of ranking a list of diseases or medical conditions based on a methylation status as claimed. As such, claims drawn to the ranked listing are not enabled.

Applicants respectfully traverse the foregoing rejection. The Patent Office is apparently contending that claims 1-50 are not enabled by the present specification because the specification allegedly lacks any amount or direction as to the process of generating (1) "expert rules" for disease analysis as seen in claim 1, lines 8-9, claims 2, 14, 16, 28, 29, and 40; (2) "selecting a type of disease or medical condition based on the methylation status..."as in lines 9-10 of claims 1, 14, 28 and 40; and (3) "ranked listing of diseases [...] based on the information about the methylation status [...]" lines 11-12 of claims 1, 14, 28 and 40. Applicants respectfully disagree for at least the reasons below.

As set forth in United States v. Telectronics, Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988), the test of enablement is not whether experimentation is necessary, but rather, whether one

of ordinary skill in the art, using the disclosure of the patent application together with information known in the art, would be able to make and use the claimed invention without requiring undue experimentation. In In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the Federal Circuit held a specification to be enabling, despite the need for experimentation, since there was adequate direction and guidance. The court in Wands further stated that enablement is not precluded by the necessity for some experimentation. However, experimentation needed to practice the invention must not be undue experimentation. The key word is "undue," not "experimentation."

Consequently, the determinative question to be asked in determining whether claims 1-50 meet the enablement requirement of 35 U.S.C. 112, first paragraph, is whether there is sufficient guidance and direction in the application to enable a person of ordinary skill in the art to make and use the invention without requiring undue experimentation. Applicants respectfully contend that there is sufficient guidance and direction in the present case.

With respect to the "expert rules," the following should be considered: it is widely known and accepted that human knowledge about prediction and classification in any field can often be expressed as a set of heuristics or "rules-of-thumb." Such a set of heuristics or "rules-of-thumb" become expert rules in cases where they are used in an expert system. An example of expert rules is the following set of rules for forecasting a gale-force Mistral, which rules are part of a weather forecasting system for the Mediterranean Sea:

IF the surface pressure difference between location 1 and location 2 is LARGE

AND a surface low pressure center or through exists in the Gulf of Genoa of the southern French coast,

THEN a gale-force MISTRAL event is LIKELY.

With respect to the present application, "expert rules" for evaluation and selection of a disease type or medical condition are rules preferably formulated by a physician for selecting a disease type or medical condition. An example of such "expert rules" could be the following:

IF the temperature of a patient is ELEVATED

AND the patient has a congested nose

THEN it is LIKELY that the patient has the flu.

Thus, as shown with the foregoing example, the specification, the knowledge known in the art, and the use of the term "expert rules" provide adequate guidance for one of ordinary skill in the art to practice the invention without undue experimentation since, for each disease type or medical condition for which an expert rule should be formulated, it is apparent to the skilled person which rule-of-thumb he/she should use as an "expert rule." Any restriction on these "expert rules" with respect to a particular way of formulating these "expert rules" would be an undue restriction.

Applicants would also like to draw the Patent Office's attention to the following U.S. patents from which the term "expert rules" and its meaning(s) can easily be derived: U.S. Patent No 5,511,004 (Dubost, et al.), U.S. Patent No. 5,537,590 (Amado) and U.S. Patent No. 6,081,786 (Barry et al.).

Furthermore, Applicants would like to draw the Patent Office's attention to pages 11-14 of the present specification wherein a large number of diseases associated with a modified methylation pattern are identified. It is respectfully submitted that one of ordinary skill in the art could use this type of information, without undue experimentation, to devise expert rules for identifying a disease based on a methylation pattern.

Therefore, in view of the above, there is a clear and direct teaching for the skilled person with respect to the formulation of "expert rules."

With respect to "selecting a type of disease or medical condition based on the methylation status...," the following should be considered: there is a finite number of disease types or medical conditions that can be diagnosed on the basis of methylation status. These types of disease or medical conditions can be taken from any standard book for diagnosis on the basis of the methylation status. As one may take from claim 1, lines 8-10, the "expert rules" are used for selecting a type of disease or a medical condition based on the methylation status. Thus, the parameters required by the Examiner on page 3, third paragraph of the subject Office Action, on which the selection of the disease or medical condition is based, are actually the expert rules. In other words, depending on the expert rules used, the type of disease or medical condition is selected. Here, the expert rules include a selection of a type of disease or medical condition based on the methylation status.

Thus, after the formulation of adequate expert rules or rules-of-thumb with respect to diseases or medical conditions based on the methylation status, the person skilled in the art is clearly enabled to select a type of disease or medical condition. Thus, the specification provides adequate guidance such that one of ordinary skill in the art can practice the invention without requiring undue experimentation. A further detailed example in the application is unnecessary to satisfy the enablement requirement since the abstract example shown and used in the specification provides sufficient direction and guidance to the person of ordinary skill to make and use the invention without requiring undue experimentation.

With respect to "ranked listing of diseases [...] based on the information about the methylation status [...]" the following should be considered: it is true that neither the claims nor the

specification require any direct explanation as to how the stated elements are to be ranked. Thus, they may be ranked with the most probable of the diseases ranked first or the least probable of the diseases ranked first. However, considering the use of the present invention, it is obvious that a person with ordinary skill in the art would rank the listing of diseases such that the most likely disease would be listed first. This is a clear and inherent feature of any system using expert rules. Thus, claims drawn to the ranked listing are enabled since the specification gives enough guidance and direction for a person of ordinary skill in the art to make and use the invention without undue experimentation.

In view of the above, Applicants respectfully submit that there is sufficient guidance and direction in the specification that a person of ordinary skill in the art would be able to make and use the claimed invention without requiring undue experimentation.

Accordingly, for at least the above reasons, the foregoing rejection should be withdrawn.

Claims 1-50 stand rejected under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In support of the rejection, the Patent Office states the following:

> Claims 1-50 are vague and indefinite in the manner of the non-sequential steps of the claims. For example claim 2 recites a third and fourth knowledge base without making clear how these limitations relate to claim 1. In addition, claim 2 states a step (C) without reciting a step (A) or (B). Claim 1 appears to recite the step (A) and (B), yet it is unclear if step (C) is to occur after the third and fourth knowledge, or after claim 1's step (B). The confusing steps of methodology are seen throughout the claims. The claims as a whole are structurally confusing.
>
> Claim[s] 1, 14, and 28 are vague and indefinite for failing to recite a final process step which agrees back with the preamble. While minor details are not required in method/process claims, at

> least the basic steps must be recited in a positive, active fashion. See *Ex parte Elrich*, 3 USPQ2d , p. 1011 (Bd. Pat App. Int. 1986). For example, claim 1 is drawn to a method for guiding the selection of a therapeutic treatment regimen for a patient, yet the claim recites a final step generating a list of diseases or medical conditions in a computing device. Claim 14 is drawn to a method of treatment, yet nowhere in the claim is any treatment given to the patient. The claims do not provide any final regimen selection for treatment nor an actual treatment. Claims dependent upon independent claims 1, 14 and 28 are likewise confusing.
>
> Claims 1, 2, 14, 16, 28, 29 and 40 are vague and indefinite due to the recitation of the phrase "expert rules" lines 8 of claim 1 for example. One of skill in the art would not reasonably be able to determine the metes and bounds of "expert rules" needed for the evaluation of a disease. The following claims 3-13, 15, 17-27, 30-39 and 41-50 are also indefinite due to their dependency from the indefinite claims 1, 2, 14, 16, 28, 29 and 40.
>
> Claim[s] 5 and 19 are vague and indefinite due to the lack of clarity as to where the "user-defined therapeutic treatment regimen" (line 2) is being entered and by whom.

Applicants respectfully traverse the foregoing rejection. The Patent Office has alleged that claims 1-50 are vague and indefinite in the manner of the non-sequential steps of the claims. Concerning claim 2, the Patent Office maintains that a step (C) is stated without reciting a step (A) or (B). Furthermore, according to the Patent Office, claim 1 appears to recite the step (A) and (B), yet, according to the Patent Office, it is unclear if step (C) is to occur after the third and fourth knowledge, or after claim 1's step (B).

In response, Applicants wish to remind the Patent Office that neither of claims 1 or 2 include any indication regarding the order in which the recited steps are to be carried out. The Patent Office is also kindly referred to MPEP 608.01(m) from which it can be taken that reference characters within parentheses may appear in the claims but are to be considered as having no effect on the scope

of the claims. Thus, the use of the reference characters (A), (B) and (C) cannot be considered as having any effect on the order in which the respective steps are to be carried out. Thus, the use of these reference characters cannot be seen as confusing or restricting the claims in any way.

The Patent Office has also rejected claims 1, 14 and 28 as allegedly being vague and indefinite for failing to recite a final process step which agrees back to the preamble. Concerning claim 1, the Patent Office states that "claim 1 is drawn to a method for guiding the selection of a therapeutic treatment regimen for a patient, yet the claim recites a final step generating a list of diseases or medical conditions in a computing device." In response, Applicants wish to point out that the generating of a list of diseases or medical conditions itself provides guidance of the selection of a therapeutic treatment or regimen. Having a list of diseases or medical conditions which are possible/probable, provides clear guidance for the selection of a therapeutic treatment for a regimen for a patient based on the listing.

Concerning claim 14, the Patent Office states that "[c]laim 14 is drawn to a treatment, yet nowhere in the claim is any treatment given to the patient." In response, Applicants wish to point out that the generating of a list of diseases or medical conditions in step (D) itself provides guidance for the selection of a therapeutic treatment or regimen. Having a list of diseases or medical conditions which are possible/probable, provides clear guidance for the selection of a therapeutic treatment for a regimen for a patient based on the listing.

Concerning the claims dependent upon the independent claims 1, 14, and 28, it is pointed out that these claims are in no way confusing as the respective dependent claims.

Concerning claims 1, 2, 14, 16, 28, 29, and 40, the Patent Office states that these claims are vague and indefinite due to the recitation therein of the phrase "expert rules." In response,

Applicants refer the Patent Office to the above arguments set forth in connection with the rejection under 35 U.S.C. 112, first paragraph. (For example, Applicants wish to point out that the language in question appears in the claims of U.S. Patent No. 6,081,786. The appearance of this term in an issued patent is evidence of its compliance with the second paragraph of 35 U.S.C. 112.)

Thus, as set forth in detail above, one of ordinary skill in the art would be able to determine the metes and bounds of "expert rules" needed for the evaluation of the respective diseases. Thus, Applicants kindly submit that claims 1, 2, 14, 16, 28, 29 and 40 are clear and definite.

Concerning claims 3-13, 15, 17-27, 30-39 and 41-50, the Patent Office states that these claims are indefinite due to their dependency from claims 1, 2, 14, 16, 28, 29 and 40. However, since claims 1, 2, 14, 16, 28, 29 and 40 meet the requirements of 35 U.S.C. 112, second paragraph, as set forth above, any rejection of claims 3-13, 15, 17-27, 30-39 and 41-50 based on their dependency from claims 1, 2, 14, 16, 28, 29 and 40 must fail.

Concerning claims 5 and 19, the Patent Office states that said claims are vague and indefinite due to an alleged lack of clarity as to where the "user-defined therapeutic treatment regiment (line 2) is being entered and by whom." In response, Applicants wish to point out that the way the user defines the therapeutic regimen and by whom, is not an essential element of the claims, and therefore does not need to be recited therein. The user-defined therapeutic regimen may be entered automatically by any kind of expert system, or may be entered by a physician. However, there is no requirement which would require including unnecessary features in a claim.

Accordingly, for at least the above reasons, the foregoing rejection should be withdrawn.

It is respectfully submitted that the present application is in condition for allowance. Prompt and favorable action is earnestly solicited.

If there are any fees due in connection with the filing of this paper that are not accounted for, the Examiner is authorized to charge the fees to our Deposit Account No. 11-1755. If a fee is required for an extension of time under 37 C.F.R. 1.136 that is not accounted for already, such an extension of time is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Kriegsman & Kriegsman

By: _____

Edward M. Kriegsman
Reg. No. 33,529
665 Franklin Street
Framingham, MA 01702
(508) 879-3500

Dated: August 15, 2002

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Box Fee Amendment, Commissioner for Patents, Washington, D.C. 20231 on August 15, 2002

_____

Edward M. Kriegsman
Reg. No. 33,529
Dated: August 15, 2002